REMARKS

Claims 37-56 are pending. Claim 42 has been canceled. Claim 56 has been added to claim subject matter originally claimed in Claim 42. Claims 37 and 50 have been amended as discussed below. Claims 48 and 51 have been amended to correct for a typographical error to replace the term "377" with the term --375-- in part (d). SEQ ID NO. 4 has 375 amino acids, not the 377 amino acids recited in originals 48 and 51. No new matter has been added by these amendments.

Claim Rejections - 35 USC §112, First Paragraph

35 U.S.C. §112, first paragraph

Claims 37-55 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one of skill in the art that the inventor had possession of the claimed invention at the time the application was filed. Specifically, the Examiner asserted that the scope of the claims includes numerous structural variants in a highly variant genus. The Examiner also asserted that the functional characteristic of eliciting antibodies is not one which identifies members of a genus. Additionally, the Examiner submits that the disclosure in the specification regarding use of anti-BVp42 antibodies to inhibit growth of parasites in vivo provides support only for the particular protein identified in the Examples.

Applicant has amended claim 37 to recite an isolated p42 polypeptide that shares at least 80% sequence identity with a polypeptide according to SEQ ID NOs. 2-5. Support for the amendment can be found on page 9, lines 3-34 of the specification. Claim 37 has also been amended to recite that the combination of said adjuvant and said isolated p42 polypeptide is capable of inducing an effective immune response against a *Plasmodium* infection in a mammal. Support for this amendment can be found throughout the specification, particularly on page 12, lines 30-35, page 29, lines 12-29 and in the Examples. Claim 50 has been similarly amended. New claim 56 contains similar language.

Applicant submits that the claims as amended satisfy the written description requirement under 35 U.S.C. §112, first paragraph. The requirements that the polypeptide exhibit at least 80% identity to a polypeptide according to any one of SEQ ID NOs. 2-5 and that the combination of said adjuvant and said isolated p42 polypeptide is capable of inducing an effective immune response against a *Plasmodium* infection in a mammal.defines a set of polypeptides that does not have substantial variation. The specification defines a functional characteristic, that of inducing an effective immune

response, and sets forth an assay for determining when the immune response has been induced.

Applicant reiterates the arguments in set forth in Applicant's Response to Office Action filed on March 21, 2003 (Paper 21) regarding the immunogenicity of the p42 polypeptide, the ability to elicit antibodies that are cross reactive between different gp 195 antigens, and effectiveness of the p42 polypeptide in vaccines.

Additionally, the Applicant submits the Declaration of inventor Sandra Chang, Ph.D. in support of the positions presented in this Response. Specifically, as set forth in paragraph 6 of Dr. Chang's Declaration, the genus of *Plasmodium falciparum* gp195 alleles (and hence corresponding p42 polypeptides) is not so large as to render the claims beyond the scope of the specification. The C-terminus of the merozite surface protein (gp195) from 15 different isolates of *Plasmodium falciparum* from Africa, Asian and Latin America possess only a few nucleotide changes leading to amino acid alterations at only four positions out of 102 residues. (Declaration at paragraph 6.) Similarly, gp195 alleles in 60 isolates from Brazil and 37 from Vietnam, possess only five single nucleotide polymorphisms in a 19 kDa region at the C-terminus. (Declaration at paragraph 6.) Additionally, there are only two known gp195 alleles. (Declaration at paragraph 6.)

The specification discloses p42 polypeptides from 4 different isolates of *Plasmodium falciparum* designated FUP, MAD, WEL and K1 representing both of the known gp195 alleles. The first allele, designated the MAD allele, is represented by the p42 polypeptides isolated from the FUP and MAD isolates. The second allele, designated the Wellcome-K1 allele, is represented by the p42 polypeptides isolated from Wellcome and K1 isolates. These isolates show high homology as between the specific alleles : there is 98% homology between the FUP and MAD isolates and 97% homology between the Wellcome and K1 isolates. (Declaration at paragraph 7.) In addition, as disclosed in Example 11, Southern blot hybridization using probes for the two alleles revealed that FUP and three other isolates designated Pf857, FVO and Hond-1 were characterized as having either the MAD allele or the K1 allele. This data illustrates the highly homologous nature of the disclosed p42 polypeptides. (Declaration at paragraph 7.)

Furthermore, the examples set forth in the Written Description guidelines and the cases cited by the Examiner to support his rejection of the present claims pertain to polypeptides that are claimed by their enzymatic or other comparable activity. The Examiner's concern regarding the effect of minor variation in sequence are misplaced in the present case since the p42 polypeptides are claimed for their immunogenic qualities, not for their enzymatic (or other) activity. As set forth in the evidence and Examples of the specification, the p42 polypeptides from the isolates each elicit antibodies that are

cross-reactive with other p42 polypeptides. (Declaration at paragraph 8.) This cross-reactivity allows the antibodies to be functionally effective against various *Plasmodium falciparum* infections. (Declaration at paragraph 8.) Previous studies have shown that, despite variation in primary structure, there is a conservation of the three-dimensional structure as between the gp195 proteins from the various *Plasmodium falciparum* isolates. (Declaration at paragraph 8. Also, see, Chang, et al., "Plasmodium falciparum: Gene Structure and Hydropathy Profile of the Major Merozoite Surface Antigen (gp195) of the Uganda-Palo Alto Isolate" *Experimental Parasitology*, 67: 1-11 at pages 5-6 (1988) and Hui, et al. " Induction of Antibodies to the Plasmodium falciparum Merozoite Surface Protein-1 (MSP1) by Cross-Priming with Heterologous MSPs" *J. of Immunology*, 153: 1195-1201 (1994), copies of each are enclosed as Exhibits A and B and are also submitted in the accompanying Supplemental Information Disclosure Statement.) Such structural conservation, in view of the cross-reactivity between antibodies, suggests that the ability of the gp195 proteins to induce an effective immune response against a *Plasmodium falciparum* infection is more dependent on the overall conformation of the polypeptides than on the primary sequence. (Declaration at paragraph 8.) As such, one would not expect that one or even several amino acid changes in the p42 polypeptides would affect their ability to induce an effective immune response. (Declaration at paragraph 8.)

One of ordinary skill in the art would conclude that the Applicant was in possession of the claimed genus at the time of filing the present application. Accordingly, Applicant requests withdrawal of the rejection of claims 37-55 under 35 U.S.C. §112, first paragraph.

CONCLUSION

Applicant respectfully submits that the Claims are in condition for allowance. If, upon review, the Examiner feels there are additional outstanding issues, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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